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CONFIDENCE BANDS FOR LOGISTIC REGRESSION WITH RESTRICTED PREDICTOR VARIABLES

Walter W. Piegorsch and George Casella *

Confidence bands are constructed for the logistic response function when there is an interval restriction on each of the predictor variables. Scheffé's S-method is employed. Specific details are given for the case of one predictor variable, along with details for a fixed-width alternative to the S-method bands. In the one-predictor case, Monte Carlo results suggest that both bands are conservative for small sample sizes, such as N=25. By N=200 the S-method's coverage probabilities are seen to attain their nominal levels while the fixed-width bands remain conservative. The procedures are exemplified with data from a short-term mutagenicity experiment.

KEY WORDS: Simultaneous inference, quantal response.

* Walter W. Piegorsch is a Mathematical Statistician, Biometry and Risk Assessment Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709, and George Casella is Associate Professor, Biometrics Unit, Cornell University, Ithaca, NY 14853. The authors thank Gregg E. Dinse and Barry H. Margolin for their careful readings of the manuscript.

1. INTRODUCTION

The analysis of dichotomous response data has been augmented in recent years by the increasing use of the logistic function to model the response probabilities. The use of the logistic model in the biological sciences dates back over 40 years (Berkson, 1944). Today it enjoys a wide variety of applications; e.g. as a failure time/survival model (O'Quigley and Struthers 1982, Abbott 1985), or in dose-response quantal assay (Morgan 1985).

In those cases where the dichotomous response, Y, is affected by a set of predictor variables, $x_1, x_2, \ldots, x_K$, logistic regression is often employed. The logistic model specifies the probability of response as

$$\begin{aligned} p(x) &= 1/\{1 + \exp[-(\beta_0 + \beta_1 x_1 + \cdots + \beta_K x_K)]\} \\ &= 1/\{1 + \exp[-\mathbf{x}'\boldsymbol{\beta}]\} \quad , \qquad (1.1) \end{aligned}$$

for $\boldsymbol{\beta}' = [\beta_0 \ \beta_1 \ \cdots \ \beta_K]$ and $\mathbf{x}' = [1 \ x_1 \ \cdots \ x_K]$.

Estimation of the parameters $\boldsymbol{\beta}$ can be accomplished via maximum likelihood (ML), although this requires an iterative computational method (Gaines Das and Tydeman 1980). Packaged computer programs simplify this, and commonly provide the Fisher information matrix, $\mathbf{F}$, or its inverse (the large-sample covariance matrix for the ML estimate of $\boldsymbol{\beta}$).

For inference regarding p(x), large-sample $1\text{-}\alpha$ confidence bands can be constructed around the estimated response. Band construction can be simplified by applying the logit transformation, $\phi(x) = \log_e\{p(x)/[1-p(x)]\}$. This transforms the problem to banding the linear form $\phi(x) = \mathbf{x}'\boldsymbol{\beta}$. The machinery developed for confidence band construction in the linear setting can then be directed at banding $\phi(x)$. Once this is done, the reverse transform $1/[1 + \exp\{-\phi(x)\}]$ can be applied to obtain bands for p(x). This has been accomplished with the well-known S-method (Scheffé 1953) for constructing bands around $\phi(x)$ in the simple linear case, K=1 (Brand et al. 1973, Khorasani and Milliken 1982), and for any $K \geq 1$ (Hauck 1983), with no restrictions placed on the predictor variable(s).

The bands can be applied to make simultaneous confidence statements on the response at different levels of x, or to form inverse confidence intervals for, say, dose levels at a given response (Carter et al. 1986), or to make comparative statements about the intersection of different response curves.

For the linear model, some research has considered restricted regions for x over which to construct the confidence band. S-method bands on $\phi(\mathbf{x})$ have been restricted to the positive orthant $\{x_i: x_i \geq 0, i=1,\ldots,K\}$ by Bohrer (1967), and then to ellipsoidal regions for x by Halperin and Gurian (1968). Casella and Strawderman (1980) later derived restricted bands over a wide class of regions for x. They noted that experimental interest is usually directed at interval restrictions on x; this would suggest restricted regions of the form

$$R_x = \{f_1 \leq x_1 \leq g_1 , f_2 \leq x_2 \leq g_2 , \ldots , f_K \leq x_K \leq g_K\} \quad , \qquad (1.2)$$

where f_i and g_i, i=1,...K, are pre-specified constants. They then showed how to embed regions of this form in their general class of restricted regions.

Interval restrictions on x are usually based upon constraints that appear within the structure of the experiment under study. Aside from directing attention to the experimental setting, restricted confidence bands enjoy the desirable property of being narrower than their unrestricted counterparts. This narrower structure can enhance predictive inference on the mean response. For example, consider the quantal data in Table 1.1. These data (LaVelle 1986) were obtained from a fluctuation assay, which is a bacterial assay used to evaluate the ability of chemicals to induce heritable DNA damage. (Discussion of this mutagenicity assay and its statistical characteristics can be found in Collings, Margolin, and Oehlert, 1981.) Doses of the suspected mutagen, 9-Aminoacridine, were applied over a wide range, 0.8 - 80 μM, and were varied logarithmically. (The first data pair in Table 1.1 corresponds to a zero-dose control. The log-dose value for this datum was calculated using consecutive-dose average spacing [Margolin, et al. 1986]).

One could construct confidence bands over all real (dose) values about a logistic dose-response for these data. In such an experiment, however, there would be greater interest in the nature of the mean dose-response over selected dose intervals. For instance, since toxic substances are often encountered at very low dose levels, interest might be directed between zero and the lower doses tested (here, 0.8 or 2.4 μM). Rather than report simultaneous confidence limits over the entire real line, it is clearly of interest to report narrower limits over pertinent, constrained regions.

No methodology has been proposed for banding p(x) under (1.1) when constraints exist on the predictor variables, and an exact approach for constraint regions other than ellipsoids seems unattainable. The Casella and Strawderman (1980) results can be applied to this problem, however, and details for this application are given in Section 2. Specifics and small-sample coverage results for the simple linear case, K=1, appear in Section 3, where application of fixed-width alternatives to the S-method bands are also discussed. Section 4 notes some further applications.

2. RESTRICTIONS ON THE PREDICTOR VARIABLE

Equation (1.1) gives the probability of response as $\Pr[Y = 1] \equiv p(\mathbf{x}) = [1 + \exp(-\mathbf{x}'\boldsymbol{\beta})]^{-1}$. Denote the ML estimator of $\boldsymbol{\beta}$ by $\mathbf{b}$. Hauck (1983) noted that under suitable regularity conditions the large-sample distribution of $\mathbf{b}$ follows a (K+1)-variate Normal distribution with mean $\boldsymbol{\beta}$ and covariance matrix consistently estimated by $\mathbf{F}^{-1}$ [recall that $\mathbf{F}$ is the Fisher information matrix from the sample of points $(\mathbf{x}_1,y_1), \ldots , (\mathbf{x}_N,y_N)$]. Thus, asymptotically,

$$\mathbf{b} \sim N_{K+1}(\boldsymbol{\beta} \, , \, \mathbf{F}^{-1}) \quad .$$

As in Casella and Strawderman (1980), one simplifies the calculations by transforming the model to diagonalized form. Write $\mathbf{D} = \mathrm{diag}\{\lambda_i\}$ as the diagonal matrix of the (ordered) eigenvalues of $\mathbf{F}$, and $\mathbf{U}$ as the matrix of corresponding orthonormal eigenvectors. Then $\mathbf{F}^{-1} = \mathbf{U}\mathbf{D}^{-1}\mathbf{U}'$. Define

$$\mathbf{z} = \mathbf{D}^{-1/2}\mathbf{U}'\mathbf{x} \qquad \text{and} \qquad \boldsymbol{\eta} = \mathbf{D}^{1/2}\mathbf{U}'\boldsymbol{\beta} \quad , \tag{2.1}$$

where $\mathbf{D}^{1/2}$ is unambiguously defined as $\mathrm{diag}\{\lambda_i^{1/2}\}$.

Since interest in $p(\mathbf{x})$ can be translated into interest in $\mathbf{x}'\boldsymbol{\beta}$ via the logit transform, we first consider the probability statement

$$\Pr\{\ (\mathbf{x}'\mathbf{b} - \mathbf{x}'\boldsymbol{\beta})^2 \ \leq\ c^2\mathbf{x}'\mathbf{F}^{-1}\mathbf{x} \quad \forall\ \mathbf{x} \in \Xi\ \} = 1-\alpha \quad , \tag{2.2}$$

where Ξ is the restricted region for $\mathbf{x}$. (We will treat probability statements such as (2.2) as equalities, although they will be so only in the limit.) The value c^2 is a constant that allows the banding equations to achieve $1-\alpha$ coverage. If $\Xi = \mathbb{R}^K$, then c^2 would simply be the χ^2 quantile based on the S-method: $c^2=\chi^2_{K+1,\alpha}$. Under the diagonalizing transform in (2.1), (2.2) becomes

$$\Pr\{\ (\mathbf{z}'\mathbf{h} - \mathbf{z}'\boldsymbol{\eta})^2 \ \leq\ c^2\mathbf{z}'\mathbf{z} \quad \forall\ \mathbf{z} \in \Omega\ \} = 1-\alpha \quad , \tag{2.3}$$

where $\mathbf{h}$ is the ML estimate of $\boldsymbol{\eta}$, and Ω is the image of Ξ under (2.1). Casella and Strawderman achieved exact results by focusing on regions of the form

$$\Omega_r = \{\ \mathbf{z} : \sum_{m=1}^{r} z_m^2 \ \geq\ q^2 \sum_{m=r+1}^{K+1} z_m^2\ \} \quad . \tag{2.4}$$

They presented values of c^2 as a function of r, $B^2=(1+q^2)^{-1}$, and the number of x-variables, K+1, for $\alpha = 0.05$ (1980, Table 1).

However, as those authors noted, interval restrictions such as those in (1.2) cannot be recovered from regions of the form (2.4). Instead, one must embed the image of R_x within some Ω_r, then find the $r \leq K$ that produces the smallest value for c^2 for use in (2.3). In the current setting, their method can be adapted into the following algorithm:

STEP 1: Given limits such as those in R_x, find the 2^K vertices $\mathbf{v}_j = \{v_{mj}\}_{m=0}^{K}$ of the corresponding hyper-rectangle. (Notice that $v_{0j} \equiv 1$ for $j=1,2,\ldots,2^K$.)

STEP 2: Translate the $\mathbf{v}_j$ into the diagonalized setting via $\boldsymbol{\psi}_j = \mathbf{D}^{-1/2}\mathbf{U}'\mathbf{v}_j$. That is, denote the M^{th} eigenvalue as λ_M, with corresponding eigenvector $\{u_{LM}\}_{L=1}^{K+1}$, $M = 1,2,\ldots,K+1$. Then, the M^{th} element of $\boldsymbol{\psi}_j = \{\psi_{Mj}\}_{M=1}^{K+1}$ is

$$\psi_{Mj} = \lambda_M^{-1/2} \sum_{L=1}^{K+1} u_{LM}\, v_{L-1,j} \quad .$$

STEP 3: Compute the following two values from each M^{th} coordinate among all the $\boldsymbol{\psi}_j$:

$$z_M^{max} = \max_{j=1,\ldots,2^K} \{ |\psi_{Mj}| \}$$

and

$$\begin{aligned} z_M^{min} &= 0 &&, \text{ if } \min_j \{\psi_{Mj}\} < 0 < \max_j \{\psi_{Mj}\} \\ &= \min_j \{ |\psi_{Mj}| \} &&, \text{ otherwise.} \end{aligned} \qquad (2.5)$$

Notice, e.g., that z_M^{max} is the largest M^{th} coordinate (in absolute value) among all vertices' M^{th} coordinates.

STEP 4: Calculate $Q_r^2 = \sum_{M=1}^{r} (z_M^{min})^2 \Big/ \sum_{M=r+1}^{K+1} (z_M^{max})^2$ for each $r = 1,\ldots K$. If $Q_r^2 = 0$, the corresponding set Ω_r does not contain the image of R_x (for that r one would apply the unrestricted value for c^2 from the S-method: $c^2 = \chi^2_{K+1,\alpha}$). If $Q_r{}^2 > 0$, then it is the largest value for q^2 (at that r) for which Ω_r contains the image of R_x; $r=1,\ldots,K$.

STEP 5: Using $q^2 = Q_r{}^2$, enter Table 1 of Casella and Strawderman (1980) with r, $B^2 = (1+Q_r{}^2)^{-1}$, and p=K+1 to find $c_r{}^2$. (B^2 can be viewed as a measure of the size of the constraint region.) As noted above, if $Q_r{}^2 = 0$, set $c_r{}^2 = \chi^2_{K+1,\alpha}$.

STEP 6: Choose the smallest value of c^2 from among the c_r^2, $r = 1,\ldots,K$.

Given c^2 from STEP 6, the confidence band on $\mathbf{x}'\boldsymbol{\beta}$, from (2.3), is simply $\mathbf{x}'\mathbf{b} \pm c(\mathbf{x}'\mathbf{F}^{-1}\mathbf{x})^{1/2}$ $\forall\, \mathbf{x} \in R_x$. Applying the logistic model gives

$$\{\, \boldsymbol{\beta} : [\, 1 + \exp\{ -\mathbf{x}'\mathbf{b} + c(\mathbf{x}'\mathbf{F}^{-1}\mathbf{x})^{1/2} \}\,]^{-1} \leq p(\mathbf{x}) \leq [\, 1 + \exp\{ -\mathbf{x}'\mathbf{b} - c(\mathbf{x}'\mathbf{F}^{-1}\mathbf{x})^{1/2} \}\,]^{-1} \quad \forall\, \mathbf{x} \in R_x \,\}$$

as a large-sample $1-\alpha$ confidence band on $p(\mathbf{x})$.

3. EXAMPLE: SIMPLE LINEAR LOGISTIC REGRESSION

3.1. Calculations for simple linear case

In the case K=1, the computational formulae are fairly simple to present. Suppose we are given the Fisher information matrix as

$$\mathbf{F} = \begin{bmatrix} I_{00} & I_{01} \\ I_{01} & I_{11} \end{bmatrix}$$

where $I_{00} = \sum_{i=1}^{N} \sigma_i^2$, $I_{01} = \sum_{i=1}^{N} x_i \sigma_i^2$, $I_{11} = \sum_{i=1}^{N} x_i\, \sigma_i^2$, and $\sigma_i^2 = \hat{p}(x_i)[1-\hat{p}(x_i)]$ (Brand et al. 1973). The (ordered) eigenvalues of $\mathbf{F}$ are

$$\lambda_1 = \{ I_{00} + I_{11} - \Delta\}/2$$

$$\lambda_2 = \{ I_{00} + I_{11} + \Delta\}/2 \qquad ,$$

where $\Delta = [\, (I_{00} - I_{11})^2 + 4I_{01}^2\,]^{1/2}$. The corresponding eigenvectors are

$$\mathbf{u}_1 = -(2\Delta)^{-1/2} \begin{bmatrix} 2I_{01}/\{\Delta - I_{11} + I_{00}\}^{1/2} \\ (-\Delta + I_{11} - I_{00})/\{\Delta - I_{11} + I_{00}\}^{1/2} \end{bmatrix}$$

and

$$u_2 = (2\Delta)^{-1/2} \begin{bmatrix} 2I_{01}/\{\Delta + I_{11} - I_{00}\}^{1/2} \\ (\Delta + I_{11} - I_{00})/\{\Delta + I_{11} - I_{00}\}^{1/2} \end{bmatrix} .$$

If R_x is of the form $\{ x : x_0 \equiv 1 \ , \ v_{21} \le x_1 \le v_{22}\}$, we have $v_1' = [\, 1 \ \ v_{21}]$, $v_2' = [\, 1 \ \ v_{22}]$, so that the $\psi_j = D^{-1/2}U'v_j$ (j=1,2) become

$$\psi_1 = (2\Delta)^{-1/2} \begin{bmatrix} \{-2I_{01} + v_{21}(\Delta - I_{11} + I_{00})\}/\{\ \lambda_1(\Delta - I_{11} + I_{00})\}^{1/2} \\ \{2I_{01} + v_{21}(\Delta + I_{11} - I_{00})\}/\{\ \lambda_2(\Delta + I_{11} - I_{00})\}^{1/2} \end{bmatrix} \qquad (3.1)$$

and

$$\psi_2 = (2\Delta)^{-1/2} \begin{bmatrix} \{-2I_{01} + v_{22}(\Delta - I_{11} + I_{00})\}/\{\ \lambda_1(\Delta - I_{11} + I_{00})\}^{1/2} \\ \{2I_{01} + v_{22}(\Delta + I_{11} - I_{00})\}/\{\ \lambda_2(\Delta + I_{11} - I_{00})\}^{1/2} \end{bmatrix} \qquad (3.2)$$

From these we need only calculate z_1^{min} and z_2^{max}, then take

$$B^2 = [\, 1 + (\, z_1^{min}/z_2^{max})^2\,]^{-1} .$$

Casella and Strawderman (1980) do not present values of c^2 for K=1, since these values effectively appear in Wynn and Bloomfield (1971, Appendix A). The Wynn and Bloomfield tables contain values for $|c|$ as an implicit function of B^2. To find $|c|$ for r=K=1 using these tables, calculate the Wynn-Bloomfield metaparameter $\beta_{WB} = |B|/(1 - B^2)^{1/2}$, and use this to enter their tables under the column for Degrees of freedom = ∞.

3.2. Fixed-width confidence bands

Gafarian (1964) introduced a fixed-width alternative to the S-method bands for use over constraint intervals such as $v_{21} \le x \le v_{22}$. Employed in (2.3), these bands have the form

$$\Pr\{ (z'h - z'\eta)^2 \leq d^2 \quad \forall\, z \in \Omega \} = 1-\alpha \,, \tag{3.3}$$

where d^2 is simply a constant that allows the confidence level to reach $1-\alpha$. The bands are roughly parallel to $\hat{p}(x)$ over much of the range for x. They converge to zero or unit probability as $x \to -\infty$ or $x \to \infty$, respectively.

Naiman (1983) compared these Gafarian bands to the S-method bands for linear regression under a minimum average width criterion. He found that the S-method bands usually dominated the fixed-width bands when the two were constructed over hyper-elliptical constrain regions. [No formulation exists for employing the fixed-width bands over regions of the form (1.2).] We felt it would be of interest to also apply these bands to the logistic regression setting.

For the case K=1, Gafarian band construction is fairly simple. Given $v_{21} \leq x \leq v_{22}$, the steps listed in §3.1 for the S-method are again followed to produce a value for the measure B^2. Then, B^2 is again employed in determining a value of d^2: calculate the Gafarian metaparameter $C_G = (1 - B^2)^{1/2}/|B|$ (which is simply $1/\beta_{WB}$ from §3.1) and, with α, enter Gafarian's (1964) tables under the column for $N = \infty$ to find d. Square this value for use in (3.3).

There is an implicit drawback to use of the Gafarian bands in this setting: over infinitely large intervals, the bands' width diverges, i.e., $d^2 \to \infty$. This corresponds to $B^2=1$, and is a possible outcome if the constraint region for x is too wide. In these cases, the S-method dominates the Gafarian form.

3.3. Monte Carlo Evaluations

The large-sample theory used in constructing the bands in (2.3) and (3.3) suggests the need for small-sample Monte Carlo evaluations of the actual coverage level. Four values of $\boldsymbol{\beta}$ were selected to represent differing forms of the probability of response as a function of x: (a) slowly increasing, $\boldsymbol{\beta} = [-1 \;\; 0.5]'$; (b) moderately increasing, $\boldsymbol{\beta} = [0 \;\; 1]'$; (c) sharply increasing, $\boldsymbol{\beta} = [2 \;\; 4]'$; and (d) slowly decreasing, $\boldsymbol{\beta} = [-0.25 \;\; -0.5]'$.

For three different sample sizes (N=25,50,200) the predictor values were equally-spaced over two different types of restricted intervals for x (wide and narrow; see the Appendix). Pseudo-random uniform (0,1) deviates were generated on a VAX-8600 using the %LR function from the GLIM system (Baker and Nelder, 1978), and these were translated into Bernoulli variates with probability of success given by (1.1). GLIM was also used to calculate **b** and $\mathbf{F}^{-1}$ for each data set. Coverage was then evaluated using (2.3) or (3.3).

To choose the number of simulation runs, ρ, we noted that each evaluation of ρ runs would produce an estimated error, α, with variance $\mathrm{var}(\alpha) = \alpha(1-\alpha)/\rho$. Thus, near α=0.05, if we wished to evaluate the true error to less than $\pm$.005, we would set $\{.05(.95)/\rho\}^{1/2} > .005$. This gives ρ>1900, hence we used ρ=1901 for the Monte Carlo evaluations.

Tables 3.1 presents the Monte Carlo results for the S-method as <u>error</u> = 1 - (estimated coverage). It shows that the procedure is fairly conservative for the smaller sample sizes, particularly at N=25. As N grows, the S-method errors attain their nominal levels, and this occurs as early as N=50 in some cases. Also, the width of the constraint interval did not seem to affect the coverage substantively, narrow intervals producing errors almost as large as those for the wider intervals.

We performed similar Monte Carlo evaluations for the Gafarian bands. The results gave estimated coverage probabilities very near to one; this appeared independent of the underlying parametric settings, or of the nominal α-level. Also, the problem of infinite width occurred with some regularity: 46% of the simulated data sets led to $d^2 = \infty$. (These cases were considered indicative of coverage.) Upon closer inspection, we isolated a possible mechanism for this overwhelming conservatism. Even when finitely-valued, the constant d^2 is often very large, usually over twice the value of c^2 at the same level of B^2. Thus the Gafarian bands often take up an unusually large portion of the area between zero and one over the constraint region: they are too wide. Coupled with the problem of infinite widths, we concluded that these bands should be reserved for instances when there is a specific need for such a form.

3.4. Mutagenicity data

Consider again the mutagenicity data in Table 1.1. Recall that these data are the proportion of responding test wells after exposure to the suspected mutagen 9-Aminoacridine. Here, x = log(dose). A total of 96 wells were examined at each exposure level, i.e. N=576. Thus the S-method's actual coverage level should be quite close to nominal.

The ML estimates are $b_0 = -0.789$, $b_1 = 0.854$. (A likelihood ratio test for an additional, parabolic term is insignificant at the .10 level, thus additional powers of x for the logistic response were not considered.) The Fisher information values are $I_{00} = 86.46$, $I_{01} = 93.82$, and $I_{11} = 314.57$. From these values, we find $\lambda_1 = 52.83$, $\lambda_2 = 348.19$, and $\mathbf{u}_1' = [-.941 \quad .337]$, $\mathbf{u}_2' = [.337 \quad .941]$.

As noted earlier, specific interest in this experiment might be directed at the lower dose levels. Table 3.2 presents values of c^2 for interval constraints on x at low exposures. Savings in width as great as 21% over the unrestricted $\chi^2_{2,.05} = 5.99$ are indicated. Figure 1 displays the estimated logistic response and 95% S-method bands for these data over the restricted interval $-1.3 \leq x \leq 0.8$. For comparison, the unrestricted 95% S-method bands are also displayed.

4. EXTENSIONS

We have discussed the problem of banding a logistic regression function when there are constraints upon the predictor variables. Specific attention has been directed to interval constraints of the form (1.2). The confidence bands were constructed from the large-sample properties of the ML estimator, **b**. This construction depended upon the value of **b** only in a location sense, i.e., providing information where to center the bands. Alternative estimators for **β** can just as easily be employed in place of **b** when the assumption of asymptotic normality remains valid. $\mathbf{F}^{-1}$ becomes the asymptotic covariance matrix for the alternative estimator of **β**.

One instance where alternatives to the ML estimate might be considered involves cases when the predictor variables are highly collinear. Collinearity in the $\mathbf{X}'\mathbf{X}$ matrix can lead to serious complications in standard linear regression (Wold et al. 1984), including the introduction of instabilities in the parameter estimates. To correct for these problems in the logistic setting, Schaefer (1986) examined alternatives such as ridge, principal components, and Stein-type estimators. All three methods were shown to reduce mean squared error while providing greater stability in the estimation of **β**. Of the three, the ridge estimate usually faired best. Related estimation procedures that modify the ML scheme to better resist the effect of certain influential observations are also available (Pregibon 1982).

APPENDIX

Restricted Intervals for Monte Carlo Evaluations

To set values for the restriction interval endpoints, v_{21} and v_{22}, for use in the Monte Carlo evaluations of Section 3.2, we inverted equation (1.1) to produce x as a function of p and **β**; to wit, $x = \{\log_e[p/(1-p)] - \beta_0\}/\beta_1$. Then, for given **β**, we selected extreme values of p from which to produce the interval endpoints. The "narrow" intervals correspond to p=.25,.75 for v_{21}, v_{22}, respectively; the "wide" intervals correspond to p=.1,.9. Specifically, these are:

	β-vector			
Interval	[-1 0.5]′	[0 1]′	[2 4]′	[-0.25 -0.5]′
narrow	v_{21}=-0.1972	v_{21}=-1.0986	v_{21}=-0.7747	v_{21}=-2.6972
	v_{22}= 4.1972	v_{22}= 1.0986	v_{22}=-0.2253	v_{22}= 1.6972
wide	v_{21}=-2.3944	v_{21}=-2.1972	v_{21}=-1.0493	v_{21}=-4.8944
	v_{22}= 6.3944	v_{22}= 2.1972	v_{22}= 0.0493	v_{22}= 3.8944

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Table 1.1

Mutagenicity of 9-Aminoacridine in E. coli strain 343/435

log-dose	-1.374	-0.223	0.875	2.079	3.178	4.382
response	7/96	28/96	64/96	54/96	81/96	96/96

NOTE: Data are (number of responding wells)/(wells tested) (LaVelle 1986).

Table 3.1

Monte Carlo errors (1-coverage) for constrained S-method confidence bands

		β-vector			
Interval	N	[-1 0.5]′	[0 1]′	[2 4]′	[-0.25 -0.5]′
		α=0.05			
narrow	25	0.024	0.025	0.028	0.016
	50	0.032	0.035	0.040	0.030
	200	0.043	0.040	0.039	0.047
wide	25	0.025	0.027	0.026	0.024
	50	0.034	0.032	0.030	0.040
	200	0.042	0.043	0.045	0.045
		α=0.01			
narrow	25	0.002	0.002	0.005	0.002
	50	0.005	0.005	0.010	0.002
	200	0.009	0.008	0.006	0.009
wide	25	0.004	0.005	0.006	0.005
	50	0.007	0.007	0.008	0.009
	200	0.006	0.006	0.011	0.006

NOTE: At α=.05, standard error $\approx \pm.005$; at α=.01, standard error $\approx \pm.002$.

Table 3.2

Values of c^2 for the Mutagenicity Data; $\alpha = 0.05$

Restriction on x	b^2	c^2
None	1.0000	5.99
$-1.3 \leq x \leq 2.0$	0.8707	5.98
$-1.3 \leq x \leq 0.8$	0.2858	5.17
$-1.3 \leq x \leq -0.2$	0.1048	4.71

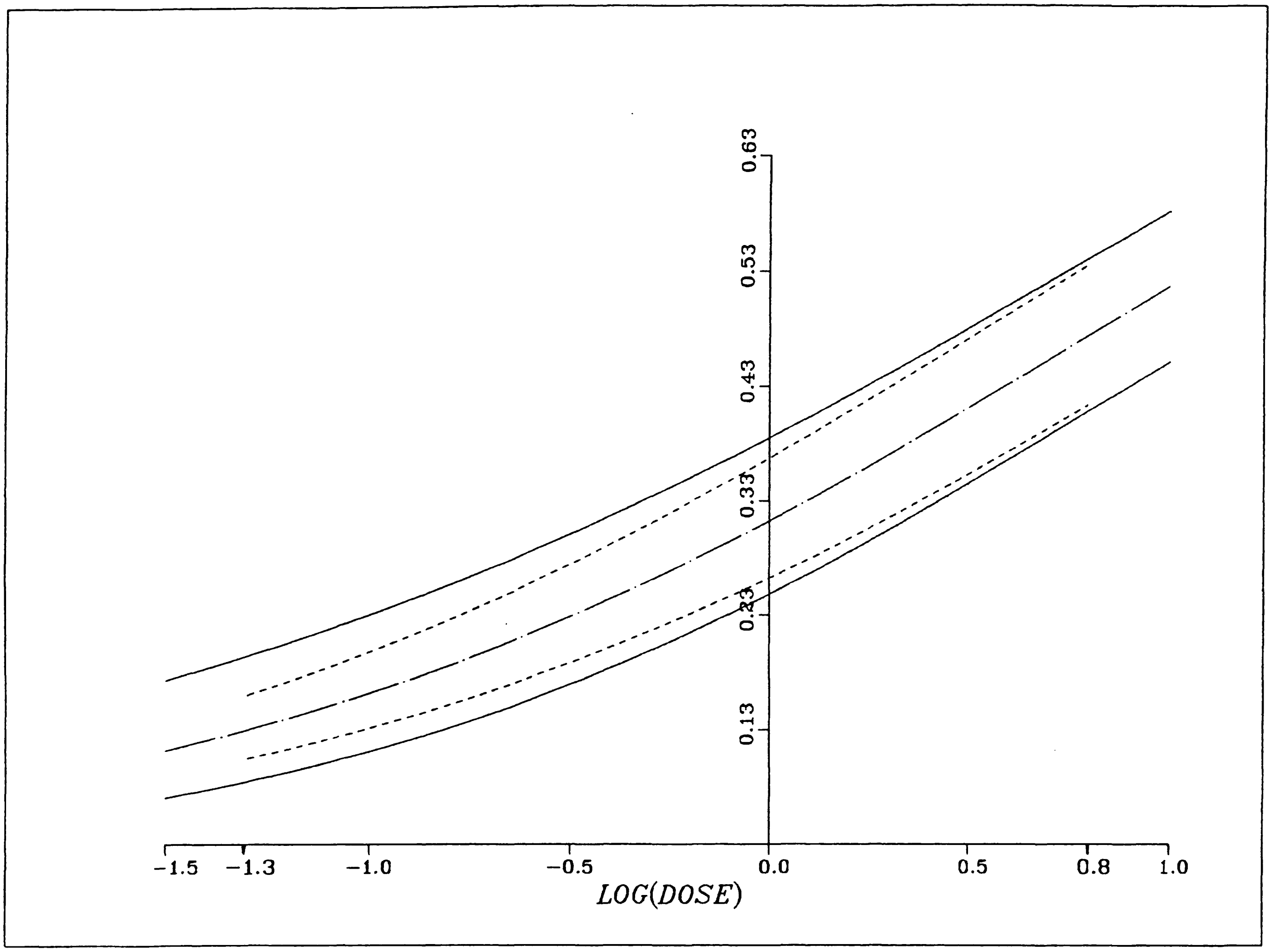

Figure 1. Estimated logistic response (—·—) and S-method bands, unrestricted (——) and restricted (---) to $-1.3 \leq x \leq 4$, for mutagenicity data from Table 1.1; α=0.05.